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Resistance of human primary mesenchymal stem cells to cytotoxic effects of nutlin-3 in vitro

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Abstract

Background: The small-molecule nutlin-3 was found to be an effective therapeutic compound and p53 activator, and acts as a murine double minute 2 antagonist, although these findings need to be clinically confirmed. The essential components of the bone marrow include mesenchymal stem cells (MSCs), which play a key role in protecting, regenerating, and proliferating hematopoietic stem cells (HSCs). This feature is vital for HSC after exposure to myelotoxic anticancer agents; nevertheless, the effects of nutlin-3 on MSCs remain to be disclosed. The present research study was conducted to examine the antiproliferative and proapoptotic effectiveness of nutlin-3 in bone marrow MSCs (BMSCs). Materials and Methods: Human-derived BMSCs were cultured for different durations, that is, 24, 48, and 72 hours, and treated using various concentrations of nutlin-3, including 5, 10, 25, 50, and 100 μM. To investigate the effect of nutlin-3 on the apoptosis, cell vitality and proliferation in BMSCs, the terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL), thiazolyl blue tetrazolium bromide, propidium iodide (PI) and annexin V assay, as well as real-time polymerase chain reaction, were used. Results: BMSCs viability significantly decreased ($P < .05$) in the cells treated at concentrations of 50 and 100 μM for 24 hours and concentrations of 25, 50, and 100 μM for 48 hours and at all concentrations for 72 hours. The apoptosis of BMSCs (TUNEL positive) was significantly more visible at concentrations of 25 and 50 μM compared with that in the controls ($P < .05$), while this increased through dose-dependent processes. Annexin V/PI staining revealed negligible dose-dependent increases in all the apoptotic cells after 72 hours of incubation, and this apoptosis elevation was significant at 25 and 50 μM ($P < .05$). Conclusion: Resistance to nutlin-3 was observed in human bone marrow–derived MSCs; nevertheless, further clinical data are required to be obtained with long-duration exposure to confirm the present findings.